Claims

1. A method for characterising a cell proliferative disorder of the breast tissues; and/or predicting the metastases free survival; and/or predicting the disease free survival; and/or predicting the response of a subject with said disorder to a treatment comprising one or more treatment which target the estrogen receptor pathway or are involved in estrogen metabolism, production or secretion, said method comprising
   a) obtaining a biological sample from the subject;
   b) determining the methylation status of one or more CpG positions within one or a combination of target nucleic acids, each of said target nucleic acids comprising essentially of all or part of the sequence of a gene taken from the group consisting of TFF1, EGR4, APC, CDKN2A, CSPG2, ERBB2, STMN1, STK11, CA9, PAX6, SFN, S100A2, TGFBR2, TP53, TP73, PLAU, TMEFF2, ESR1, SYK, HSPB1, RASSF1, TES, GRIN2D, PSAT1, CGA, CYP2D6, COX7A2L, ESR2, ~~PLAU,~~ PITX2, VTN, SULT1A1, PCAF, PRKCD, ONECUT2, BCL6, WBP11, (MX1)MX1, APP, ORC4L, NETO1, TBC1D3, GRB7, CDK6, SEQ ID NO: 47, SEQ ID NO: 48, ABCA8, SEQ ID NO: 50, SEQ ID NO: 51, MARK2, ELK1, Q8WUT3, CGB, BSG, BCKDK, SOX8, DAG1, SEMA4B, ESR1 (exon8) and/or their regulatory regions by contacting said target nucleic acid with one or more agents that convert cytosine bases that are unmethylated at the 5'-position thereof to a base that is detectably dissimilar to cytosine in terms of hybridization properties; and
   c) determining therefrom the prognosis of said subject, characteristics of said cell proliferative disorder, disease free survival and/or probability of response of said subject to said treatment.

2. A method according to claim 1, wherein in step b) the methylation status of one or more CpG positions within one or a combination of target nucleic acids, each of said target nucleic acids comprising essentially of all or part of the sequence of a gene taken from the group consisting of TFF1, PITX2 and PLAU is determined.

3. The method according to claim 1 or 2, further comprising
   d) determining a suitable treatment regimen for the subject.

4. A method according to any of claims 1 to 3, further comprising predicting the response of a subject with said disorder to a treatment comprising one or more treatment which target the estrogen receptor pathway or are involved in estrogen metabolism, production or secretion wherein said method is characterised in that the methylation status of one or more CpG positions within at least two target nucleic acids is determined wherein at least one of said target nucleic acids comprises essentially of all or part of the sequence of the gene TFF1 and wherein at least one of said target nucleic acids comprises essentially of all or part of the sequence of the gene PITX2.

5. A method according to any of claims 1 to 3, further comprising characterising a cell proliferative disorder of the breast tissues and/or a metastases thereof; and/or predicting the disease free survival wherein said method is characterised in that the methylation status of one or more CpG positions within at least two target nucleic acids is determined wherein at least one of said target nucleic acids comprises essentially of all or part of the sequence of the gene PLAU and wherein at least one of said target nucleic acids comprises essentially of all or part of the sequence of the gene PITX2.

6. The method according to any of claims 1 to 5 wherein said suitable treatment regimen comprises one or more therapies selected from the group consiting of chemotherapy, radiotherapy, surgery, biological therapy, immunotherapy, antibodies, molecularly targeted drugs, estrogen receptor modulators, estrogen receptor down-regulators, aromatase inhibitors, ovarian ablation, LHRH analogues and other centrally acting drugs influencing estrogen production.

7. A method according to any of claims 1 to 3, wherein said treatment is an adjuvant treatment and said genes are selected from the group consisting of ERBB2, STMN1, TFF1, TMEFF2, ESR1, HSPB1, PITX2, COX7A2L, PLAU, VTN, PCAF, ONECUT2, BCL6, WBP11, TBC1D3, GRB7, CDK6, SEQ ID NO: 47, ABCA8 and SEQ ID NO: 51.

8. A method according to any of claims 1 to 3, wherein said treatment is an adjuvant treatment and said target nucleic acid(s) are selected from the group consisting of SEQ ID NO: 5, 6, 12, 17, 18, 20, 23, 28, 16, 31, 33, 35, 36, 37, 43, 44, 46, 47, 49 and 51.

9. A method according to any of claims 1 to 3, wherein said disorder is a metastatic disease and said genes are selected from the group consisting of APC, CSPG2, ERBB2, STK11, S100A2, TFF1, TGFBR2, TP53, TMEFF2, SYK, HSPB1, RASSF1, PSAT1, CGA, ESR2, ONECUT2, WBP11, CYP2D6, CDK6, ELK1, CGB and DAG1.

10. A method according to any of claims 1 to 3, wherein said disorder is a metastatic disease and said target nucleic acid(s) are selected from the group consisting of SEQ ID NO: 2, 4, 5, 7, 11, 12, 13, 14, 17, 19, 20, 21, 25, 26, 29, 35, 37, 45, 46, 53, 55 and 59.

11. A method according to any of claims 1 to 10, characterised in that the genomic DNA is obtained from cells or cellular components which contain DNA, sources of DNA comprising, for example, cell lines, histological slides, paraffin embedded tissues, biopsies, tissue embedded in paraffin or sections thereof, breast tissues, blood, plasma, serum, lymphatic fluid, lymphatic tissue, duct cells, ductal lavage fluid, nipple aspiration fluid, cerebrospinal fluid, bone marrow and combinations thereof.

12. A method according to any of claims 1 to 11, wherein said cell proliferative disorder of the breast tissue is selected from the group consisting of ductal carcinoma *in situ*, invasive ductal carcinoma, invasive lobular carcinoma, lobular carcinoma *in situ,* comedocarcinoma, inflammatory carcinoma, mucinous carcinoma, scirrhous carcinoma, colloid carcinoma, tubular carcinoma, medullary carcinoma, metaplastic carcinoma, and papillary carcinoma and papillary carcinoma *in situ*, undifferentiated or anaplastic carcinoma and Paget's disease of the breast.

13. A method according to any of claims 1 to 12, wherein said subjects are estrogen and/or progesterone receptor positive.

14. A method according to any of claims 1 to 13 wherein step b) comprises
a) converting cytosine bases in the genomic DNA sample which are unmethylated at the 5-position, to uracil or another base which is dissimilar to cytosine in terms of base pairing behaviour;
b) amplifying at least one fragment of the pretreated genomic DNA, wherein said fragments comprise at least 8 base pairs of one or more sequences selected from the group consisting of SEQ ID NO: 206 to 449 and sequences complementary thereto, and

c) determining the methylation status of one or more genomic CpG dinucleotides by analysis of the amplificate nucleic acids.

15. The method according to claim 14, wherein ii) is carried out using one or both of MSP and/or HeavyMethyl.

16. The method according to claim 14, wherein iii) is carried out by means of one or more methods taken from the group consisting oligonucleotide hybridisation analysis, Ms SnuPE, sequencing, Real Time detection probes and oligonucleotide array analysis.

17. A nucleic acid molecule consisting essentially of a sequence at least 18 bases in length according to one of the sequences taken from the group consisting of SEQ ID Nos: 206 to 449.

18. An oligomer, in particular an oligonucleotide or peptide nucleic acid (PNA)-oligomer, said oligomer consisting essentially of at least one base sequence having a length of at least 10 nucleotides which hybridises to or is identical to one of the nucleic acid sequences according to SEQ ID NO: 206 to 449.

19. A set of at least two oligonucleotides as recited in claim 18.

20. A kit comprising a bisulfite (= disulfite, hydrogen sulfite) reagent as well as oligonucleotides and/or PNA-oligomers according to one of the Claims 18 or 19.

21. A kit according to claim 20, further comprising standard reagents for performing a methylation assay from the group consisting of MS-SNuPE, MSP, Methyl light, Heavy Methyl, nucleic acid sequencing and combinations thereof.

22. Use of a method according to one of claims 1 through 16, a nucleic acid according to Claim 17, of an oligonucleotide or PNA-oligomer according to Claim 18, of a kit according to Claim 20 or 21 or of a set of oligonucleotides according to claim 19 for the treatment of breast cell proliferative disorders.